Failure of passive zooprophylaxis: cattle ownership in Pakistan is associated with a higher prevalence of malaria

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Abstract

To examine the possibility that domestic cattle kept in house courtyards might protect occupants against malaria through zooprophylaxis, parasite prevalence surveys were conducted of schoolchildren in Pakistani and Afghan refugee villages and analysed according to whether each child's family kept cattle. Parasite prevalence (15·2%) was significantly greater among children of families which kept cattle than among those which did not (9·5%). Comparison of prevalence between different villages revealed a positive correlation between parasite rates and the proportion of families owning cattle. The latter finding supports the prediction of the Sota–Mogi theoretical model that domestic animals can enhance rather than reduce malaria transmission when vectors are zoophilic, the infection rate low, and the human:cattle ratio high. All these conditions applied in the study area.

Keywords: malaria, prevalence, zooprophylaxis, effect of cattle, Pakistan

Introduction

Zooprophylaxis has been defined by the World Health Organization (WHO, 1982) as 'the use of wild or domestic animals, which are not the reservoir hosts of a given disease, to divert the blood-seeking mosquito vectors from the human hosts of that disease'. It may be active or passive. Active zooprophylaxis is a reduction in malaria or human-biting resulting from the deliberate deployment of domestic animals as a barrier between mosquito breeding sites and human settlements (WHO, 1991). Passive zooprophylaxis is the serendipitous reduction in malaria purported to occur when cattle density increases within a community (see, e.g., SWELLENGREBEL & DE BUCK, 1938; GIGLIOLI, 1963).

In Pakistan, a higher incidence of malaria is recorded at health centres for Afghan refugees than at centres serving local Pakistanis. The difference was initially attributable to Afghans having been less exposed to malaria and therefore less immune during the first years after their arrival in Pakistan (SULEMAN, 1988). It has also been suggested that, because refugee families possess fewer livestock than Pakistani local residents (ENGLISH, 1989), they are less able to benefit from any zooprophylactic effect of cattle (ZULETA, 1989).

Conditions in Pakistan seem, at first sight, highly conducive to successful passive zooprophylaxis. The major malaria vectors are highly zoophilic, and Afghans and local residents prefer to keep their cattle close to their living quarters. However, a mathematical model developed by SOTA & MOGI (1989) has exposed problems with the theory: simulations predict that introduction of cattle can lead to increased vector densities, increased human biting rates, and greater malaria transmission. Appropriate deployment of cattle away from human dwellings may be crucial to the success of zooprophylaxis (SCHULTZ, 1989).

This paper reports cattle ownership and malaria parasite prevalence surveys conducted in refugee and local villages in the North-West Frontier province (NWFP) of Pakistan. It examines the relationship between cattle and malaria at the household and village levels, and assesses whether household cattle lessen or exacerbate the malaria problem.

Materials and Methods

Rural Pakistanis and Afghan refugees live in houses made from mud, surrounded by an open courtyard and high perimeter wall. Both communities keep domestic animals (cattle, water buffaloes, goats, etc.) in courtyards and sheds usually within 10 m of the living quarters. People sleep in the courtyards during summer, moving indoors from October onwards. Sources of mosquito breeding include borrow pits, river margins and rice paddies, and the fauna includes *Anopheles culicifacies*, *A. stephensi* and *A. subpictus* among others. Transmission of *Plasmodium vivax* and *P. falciparum* occurs between April and December and reaches a peak in October/November.

The study areas were 3 refugee and 4 local villages situated along a 24 km valley in Kohat district, NWFP, Pakistan, and a pair of neighbouring refugee and local villages in Mohmand, a tribal area 100 km north of Kohat. Health services were provided by the United Nations High Commission for Refugees and the Government Department of Health, both of which conduct vector control campaigns (house spraying with malathion) in July each year. According to spray reports, house coverage ranged from 82 to 100% and all study villages were sprayed.

Parasite prevalence surveys were conducted in village schools in October 1989 in Mohmand, and in November 1989 and November 1990 in Kohat. Schoolchildren were aged 4–15 years; 90% were boys. Thick and thin blood films were prepared from virtually all children present on the day of examination, stained with Giemsa's stain and examined at the Médecins sans Frontières reference laboratory. One hundred microscope fields of each film were examined before reporting a slide as negative. Parasitaemic children were given supervised treatment with chloroquine (25 mg/kg body weight in divided doses over 3 d), whether symptomatic or not. During blood collection each child was asked in private by the survey team—with the schoolteacher presiding—whether his or her family kept cattle (cows or water buffaloes) within the house compound.

Results

Parasite prevalence in households with or without cattle

Parasite prevalence was correlated with age, increasing from 10·2% at 4 years to 18·1% at 15 years. All further comparisons were therefore conducted on age-adjusted prevalence rates using the method of direct standardization (the standard population was produced from the total of all the surveys).

In Kohat the prevalence rate in the Afghan community was similar to that in the Pakistanis, whereas in Mohmand prevalence was significantly greater in Afghans ($\chi^2=18{\cdot}9$, degrees of freedom [d.f.]=2, $P=0{\cdot}0001$) (Table). Prevalence also showed geographical variation (see the data for 1989 in the Table), with *P. falciparum* predominant in Kohat and *P. vivax* predominant in Mohmand. Prevalence also varied between years, particularly that of *P. falciparum* which, in Kohat, was higher in 1990 than in 1989. Thus in order to evaluate the relationship between cattle and parasite prevalence, and avoid the potentially confounding variation between communities, localities and years, it was necessary to examine each of the 6 subsets of data separately, age-

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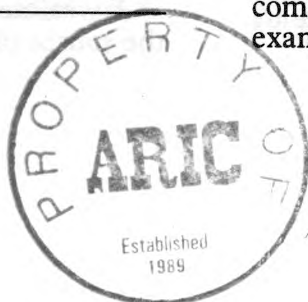


Table. Results of parasite prevalence surveys in children with or without cattle in their house courtyards; parasite rates are adjusted according to age

Locality, year, and country of origin	Cattle	No. of slides examined	No. of cases *P. vivax*	No. of cases *P. falciparum*	Parasite rate (%) *P. vivax*	Parasite rate (%) *P. falciparum*	Parasite rate (%) Both species	Mean age (years)
Mohmand (1989)								
Afghanistan	Yes	80[a]	5	8	5·3	10·1	15·3	7·8
	No	282[b]	24	11	7·8	4·2	12·0	6·9
	Both	362	29	19	7·3	5·4	12·7	
Pakistan	Yes	217	9	3	3·5	1·7	5·2	9·1
	No	182	5	0	3·3	0	3·3	9·8
	Both	399	14	3	3·3	1·1	4·4	
Kohat (1989)								
Afghanistan	Yes	204[a]	9	20	4·3	11·2	15·6	7·9
	No	208	5	13	2·4	5·9	8·3	7·3
	Both	412	14	33	3·4	9·0	12·4	
Pakistan	Yes	200	10	19	5·7	9·8	15·5	7·6
	No	42	0	6	0	14·0	14·0	7·1
	Both	242	10	25	4·8	10·7	15·5	
Kohat (1990)								
Afghanistan	Yes	184	6	38	3·2	15·4	18·5	10·2
	No	110	0	15	0	14·6	14·6	8·6
	Both	294	6	53	2·1	15·6	17·7	
Pakistan	Yes	264	10	45	3·5	17·1	20·6	8·3
	No	69	2	7	2·0	6·9	8·9	9·1
	Both	333	12	52	3·4	15·9	19·3	
Totals	Yes	1149	49	133	4·1	11·1	15·2	8·5
	No	893	36	52	3·9	5·7	9·5	8·0

[a]Includes one mixed infection.
[b]Includes 2 mixed infections.

adjust each one with reference to the standard population, and use the Mantel–Haenszel (M–H) χ^2 test to summarize the evidence. The analysis showed that prevalence was significantly greater in children with cattle (mean prevalence=15·2%) than in children without cattle (mean prevalence=9·5%) (M–H $\chi^2=9{\cdot}6$, d.f.=1, $P<0{\cdot}005$). This trend was consistent in 5 of the 6 subsets, with both *P. falciparum* (M–H $\chi^2=7{\cdot}2$, d.f.=1, $P<0{\cdot}01$) and *P. vivax*, though the latter result was not significant by itself (M–H $\chi^2=1{\cdot}7$, d.f.=1, $P>0{\cdot}05$).

Cattle ownership was less common among refugees than local people and less common in Mohmand than Kohat. In Mohmand, 22% of refugees kept cattle compared to 54% of local residents. In Kohat, 55% of refugees kept cattle compared to 81% of local inhabitants. The human:cattle ratio in refugee villages was 5·8 in Kohat and 11·6 in Mohmand.

Parasite prevalence and percentage ownership of cattle in different villages

The mean age-adjusted prevalence rate and the mean proportion of children keeping cattle were calculated for each Kohat village from the 1989 and 1990 survey data. Prevalence increased by an average of 7·7% (range 0·1–19·5%) between 1989 and 1990, and the children's response to the question of cattle ownership differed by an average of 7·0% (range 4·6–11·2%) between the 2 years. The mean parasite rates and proportions keeping cattle were positively correlated ($r=0{\cdot}79$, $F(1,5)=8{\cdot}09$, $P=0{\cdot}036$) (Figure).

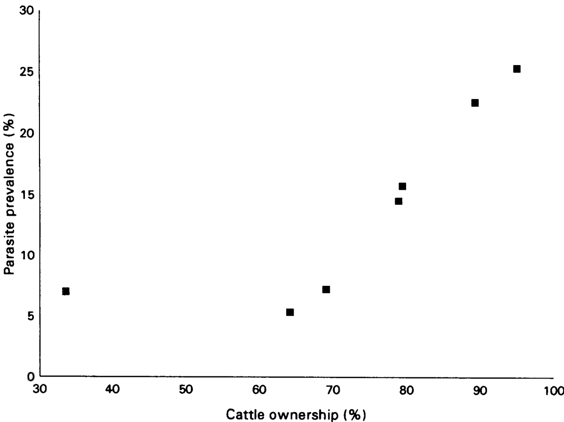


Figure. Comparison of malaria parasite prevalence in village schoolchildren and the percentage of families keeping cattle. Each point represents the mean of 2 surveys conducted in 1989 and 1990 in 7 villages in Pakistan. Prevalence rates in each survey were age-adjusted with reference to a standard population.

Discussion

Cattle ownership and parasite prevalence were associated in 2 ways. Families which kept cattle in their house courtyards recorded a higher prevalence than families which did not (the 'compound effect'). Villages with a greater proportion of cattle-owning families recorded a higher prevalence than villages with fewer cattle-owners (the 'village effect').

The compound effect was the opposite of that predicted by classical zooprophylaxis theory. Recent experiments by HEWITT *et al.* (1994) in a refugee village may provide the explanation: these showed that biting rates on sleeping people increased if cattle were kept in the vicinity. It seems that mosquitoes are indeed attracted to cattle, but instead of being diverted away from human hosts may encounter and feed upon sleeping humans *en route* to cattle. It follows that, if the biting rate on cattle-owning families is greater, malaria prevalence should also be higher in that group.

The mere rearrangement of mosquitoes within a village is unable to explain the area effect or to replicate the results shown in the Figure. That would require an increase in the number of mosquitoes per person. In the model developed by SOTA & MOGI (1989), mosquito densities increase when cattle are introduced because cattle constitute a readily accessible source of blood. Under certain conditions this can lead to greater human-biting rates and higher vectorial capacity, and thus the Sota–Mogi model was able to predict the village effect results. The prerequisites for increased transmission in the Sota–Mogi model are that growth of mosquito populations should be unconstrained, the vectors zoophilic, the infection rate low, and the ratio of humans to cattle high. In Kohat, river beds and paddies provide abundant breeding sites, the major vectors *A. culicifacies* and *A. stephensi* are highly zoophilic (REISEN & BOREHAM, 1982), transmission is seasonal, and the lowest estimate of the human:cattle ratio was 5·8. Thus conditions seem consistent with those of the model.

A weakness in the study is that children were used as the source of information on cattle ownership. However,

the method of direct inquiry, presided over by the schoolteachers, may not be so unreliable, since the proportion of children claiming cattle ownership differed by only 7% between the 2 years. Moreover, any inaccuracy would tend to bias against the observed results.

Apart from cattle, we were unable to identify any factor that might be responsible for the observed effects. The low incidence of malaria in urban areas, for example, though correlated with low cattle densities, is probably caused by breeding site scarcity and less-efficient vector species (REISEN & MILBY, 1986). Kohat, however, is uniformly rural with small scattered villages. Wealth and cattle are also associated, but one would expect wealthier, presumably better-educated, cattle-owners to record a lower rather than higher prevalence as a result of self-medication with antimalarial drugs.

Our original assumption that malaria was more common in refugees received no support from the results of the Kohat prevalence surveys. In this district some refugee villages had just as many cattle as Pakistani villages and the prevalence rates reflected percentage cattle ownership rather than local or refugee status. However, in the poorer, more arid tribal areas of Mohmand, Pakistanis recorded a lower prevalence than refugees despite owning more cattle. Breeding sites around the Pakistani village were scarce, and may have limited any expansion of the mosquito population, a prerequisite of the village effect.

Current livestock management practices in Pakistan appear to exacerbate the malaria problem. According to the Sota–Mogi model, cattle would reduce the mosquito human-biting rate only if very large numbers were introduced. In Pakistan that seems unlikely, for economic reasons. A change in livestock management, so that cattle were kept between village and breeding site, might prove zooprophylactic (WHO, 1991). But such a practice would probably be unacceptable—cattle are too valuable to be kept outside the compound—and would require almost total community participation to be effective. Current investigations into insecticide dips and insecticide-impregnated ear tags for cattle may offer some solutions.

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Recruitment to a trial of tuberculosis preventive therapy from a voluntary HIV testing centre in Lusaka: relevance to implementation

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Abstract

To determine the number of clients attending for voluntary human immunodeficiency virus (HIV) testing who are able to enter a trial of preventive therapy for tuberculosis, and the factors that determine who receives therapy, we studied 475 consecutive people attending for an HIV test at Lusaka's first voluntary HIV testing centre and the preventive therapy study clinic at the University Teaching Hospital, Lusaka, Zambia. Semi-structured interviews were conducted by counsellors and collated with recruitment data from the trial. Two hundred and twenty-five people were seropositive, of whom 201 returned to collect their results; 77 (38%) of these (16% of the total number screened) entered the trial. Reasons for not entering the trial included exclusion by trial protocol (30), including 18 who had active tuberculosis; psychological adjustment to a positive result (27); death (6); worries about confidentiality (3); the experimental nature of the trial (12); attitudes of staff in the hospital (5); and cost of transport (7). Targeting preventive therapy at those who are already choosing to be tested for HIV seems appropriate and may be cost-effective. Although visiting a hospital may deter some people, the prevalence of active tuberculosis among this group emphasized the importance of arranging adequate screening facilities.

Keywords: tuberculosis, human immunodeficiency virus, drug trial recruitment, Zambia

Introduction

The incidence of tuberculosis among people infected with both *Mycobacterium tuberculosis* and human immunodeficiency virus (HIV) is between 3% and 8% per year (SELWYN *et al.*, 1989; BRAUN *et al.*, 1991), with reactivation of latent infection as an important mechanism. In sub-Saharan Africa, where both infections are prevalent, tuberculosis control programmes are already overstretched. In Zambia, most of the adult population are infected with *M. tuberculosis* (see DUNCAN *et al.*, 1995) and the prevalence of HIV infection among women attending antenatal clinics in periurban Lusaka is 33% (Zambian Ministry of Health unpublished figures, 1992; n=976). The incidence of tuberculosis has risen from around 100/100 000 in 1984 to over 300/100 000 in 1993 (Ministry of Health figures), and in 1989 73% of patients receiving antituberculous therapy were seropositive for HIV (ELLIOTT *et al.*, 1993). Preventive therapy with a one-year course of isoniazid reduced the incidence of tuberculosis over the subsequent 5 years in people with HIV infection in Haiti (PAPE *et al.*, 1993) and preliminary results using a 6 months' regimen in Zambia were similar (WADHAWAN *et al.*, 1991). Since 1992, a trial of 2 different preventive therapy regimens has been running in Lusaka (MWINGA *et al.*, 1993).

Possible strategies for using such treatment on a larger scale need to consider how to find people who are infected with HIV. The cost of screening people for HIV antibodies, specifically to offer them tuberculosis preventive therapy, is likely to be prohibitive but will depend on the prevalence of HIV in the community targeted and on the number of people who cannot receive therapy for whatever reason. However, if voluntary HIV testing centres become established for reasons other than tuberculosis control, it may be feasible to offer preventive therapy to those found to be seropositive.

Since 1985, when the HIV antibody test was first licensed, the demand for counselling and testing has steadily increased. In the USA, where testing has been carried out since 1985, more than 2 000 000 tests were carried out in public-funded sites in 1991 (CDC, 1992). Counselling and testing have been used to help people assess their risks, to encourage or reinforce behaviour change, to refer infected individuals to clinical care, and to start antiviral or preventive therapy when needed. Some longitudinal studies of homosexual men have found that those who are seropositive show greater reductions in risky behaviour than those who are not (HIGGINS *et al.*, 1991).

In sub-Saharan Africa, where HIV infection is prevalent and medical resources are scarce, the role of counselling and testing is less obvious (COLEBUNDERS & NDUMBE, 1993). Demand for such services exists, and between June 1991 and October 1992 the AIDS Information Centre in Kampala, Uganda, tested more than 30 000 people (AISU *et al.*, 1995). Studies in Africa have also demonstrated changes in sexual behaviour that would be expected to reduce transmission of HIV (ALLEN *et al.*, 1992). There may also be other benefits to people who receive counselling such as an increase in 'coping' mechanisms. Antiviral therapy is too expensive for general use in Africa, but preventive therapy against tuberculosis might not only be more cost-effective than treating tuberculosis when it develops but may also reduce transmission of *M. tuberculosis* in the community and prolong the life of dually infected individuals.

The first voluntary HIV counselling and testing centre in Zambia was established by the Kara–ZAMBART project to meet a perceived demand, to help with coping and to determine whether behaviour was being altered (BAGGALEY *et al.*, 1993). Whatever the result, people are encouraged to avoid risky behaviour, in order to reduce transmission or to remain uninfected. People found to be HIV-seropositive are also encouraged to enter the preventive therapy trial.

We have looked at the number of clients entering the trial and the reasons for failure so to do, in order to explore the likely constraints on widespread implementation of preventive therapy for tuberculosis.

Methods

The study was conducted at the Kara–ZAMBART Voluntary HIV Counselling and Testing Project and at the University Teaching Hospital (UTH) in Lusaka, Zambia.

ZAMBART tuberculosis preventive therapy trial

This trial is a collaborative project between the Department of Medicine at UTH, the Ministry of Health in Zambia and the London School of Hygiene and Tropical Medicine, comparing the efficacy of preventive therapy against tuberculosis with 6 months' intermittent iso-

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